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An overview of nano formulated heavy metal and its toxic effect on Zebra fish (Danio rerio) embryos

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ABSTRACT:

Nanoparticles due to their needs and applications of nanomaterials in the different areas like industry, agriculture, medicine results in release of nanoparticles into the aquatic environment. Hence the study their effects of these nanoparticles should be assessed which can cause damage to the aquatic environment. This review states the investigation of metal nanoparticles such as silver, gold, silica, zinc, titanium and metal oxide nanomaterials like zinc oxide, iron oxide and their toxic effects and behavioral changes in the zebra fish embryos. The experimental results showed that the NPs inhibited the hatching rate of the zebra fish larvae and the toxicity is also dose dependent. Hatching delay and some changes like reduced body length of the larvae, defective eye development and tail malformation sometimes death of the embryo also seen.

Key words: Zebra fish embryo, Nanoparticles, hatching rate, toxicity.

INTRODUCTION:

Nanotechnology has great deal of interest due to their needs and applications of nanomaterials in many areas of human endeavors such as industry, agriculture, business, medicine, public health amongst many others. (Ju-Nam, Y et al , 2008) (Oberdorster et al, 2014) recently published the first report about manufactured nanomaterials (MNMs) imperiling an aquatic organisms health and could exert oxidative stress and cause severe lipid peroxidation in fish brain tissue. Another recent study examining the effect of nC60 on freshwater crustaceans noted that after 21 d of exposure, Daphnia magna had a delay in molting and a significant decrease in offspring production at 5 mg/L (Oberdorster 2006) The mortality of Daphnia organisms also was reported to increase with nC60 concentration (Lovern et al 2006). These studies reflect the importance of considering the potential environmental impacts of such nanolitter. Nanomaterials possess unique physical and surface properties, which have inspired plans for a wide spectrum of applications, such as target-specific vehicles for in vivo sensing, diagnosis, and therapy (e.g., nanomedicine and drug delivery) (Tiwari, S,Xu.X.H.N et al2004,2005,2007,Yamada 2003) These unique properties may also incite toxicity, damaging in vivo systems of interest and posing risks to human health and the environment.(Nel et al 2006) Increasing use of nanomaterials is resulting in their release into the environment, making necessary to determine the toxicity of these

materials.(unnai vicario2008) Due to their small size and consequent large number of surface atoms per mass unit, nanoparticles (NPs) possess unique mechanical, catalytic and optical properties as well as electrical conductivity when compared with their bulk counterparts (Niemeyer 2001; Oberdo ¨rster et al. 2005). These unique properties make them suitable for many industrial processes, and consequently, manufactured NPs are currently used in different areas, such as electronics, biomedicine, pharmaceuticals, cosmetics, environmental analysis and remediation, catalysis and material sciences (Nowack and Bucheli 2007; Ju-Nam and Lead2008). Results indicate that nano-sized metals can cause both lethal and sub lethal effects on developing fish, which include increased mortality, abnormal development and hatching rate reduction (Shaw and Handy 2011). Specifically, metal oxide NPs cause different toxic effects, including tissue damage, acute lethality or induction of ROS production (Lin et al. 2011; Zhao et al. 2013; Lieschke GJ2007) Zebrafish have been used predominantly in developmental biology and molecular genetics, but their value in toxicology as well as drug discovery has been recognized. To evaluate the toxicity of a chemical, it is essential to identify the endpoints of toxicity and their dose-response relationships, elucidate the mechanisms of toxicity, and determine the toxic dynamics of the chemical. (Adrian J. Hill 2005)

Toxicity of ZnO nanoparticle;

Wei Bai et al 2009 reported that ZnO nanoparticles are commonly applied in optoelectronics, cosmetics, catalysts, ceramics, pigments, etc. Previous reports said that nano-ZnO was biosafe and biocompatible and could be applied in biomedical materials. Nano-ZnO was predictable as a respiratory toxicant which caused metal fume fever (myalgia, cough, fatigue, etc.) .Zebra fish embryo has been proved to be a good model vertebrate to assess the toxicity of nanoparticles. Compared with the conventional toxicology, the dose is no longer a only factor in evaluating the toxicity of nanoparticles. Zebrafish 96-h post fertilization (hpf) embryo–larval test was performed to assess the toxicity of nano-ZnO suspension. The physicochemical properties of nanoparticles, such as size, shape, chemical composition, aggregation, etc., need to be taken into account in aquatic toxicity testing. Moreover, the pH and salinity of the aqueous exposure system are also important factors. Unlike insoluble nanoparticles such as nano-TiO2 and nano-SiO2, the solubility of nano-ZnO may play a more important role in its toxicity. Comparative experiments showed that nano-. ZnO suspension, small aggregates, Zn (dis), and large aggregates might jointly exert influence on the development of zebrafish embryos. The embryo toxicity test revealed that nano-ZnO killed zebrafish embryos (50 and 100 mg/L**)**, retarded the embryo hatching (1–25 mg/L), reduced the body length of larvae, and

caused tail malformation after the 96 hpf exposure. Zn (dis) only partially contributed to the toxicity of nano-ZnO.

Toxicity of metal oxide nanoparticles (CuO, ZnO and TiO2)

Unai Vicario-Pare ´s et al 2014 reported that CuO NPs are used as additives in lubricants, in computer processors, conductive coatings, printer inks and cosmetics, and as antimicrobial agent. These NPs have already been shown to be toxic to different organisms producing oxidative stress and DNA damage. In zebrafish, embryo exposure to CuO NPs reduces hatching rate at concentrations higher than 0.5 mg CuO/L .Ionic copper affected hatching in a more severe manner, reducing the percentage of hatched embryos and delaying hatching at concentrations in the range 0.1–10 mg/L.

ZnO NPs are applied in electronic sensors, solar voltaic devices as well as in the production of sunscreens, cosmetics, paints, ceramics and fungicides or in wastewater treatment. Previous studies in zebrafish embryos have shown that ZnO toxicity is dose-dependent and similar for the nanoparticulate and bulk forms, although inconsistent results appear in the literature. Regarding the hatching parameters, ZnO NPs produced significant reduction of the percentage of hatched embryos only at 10 mg Zn/L.

TiO2 NPs, the most commonly used NPs, are very useful in photo catalysis, in environmental technology for the treatment of wastewater and ground water and for the degradation of air pollutants, and are also used in the production of sunscreens and cosmetics. TiO2 exists in different structural forms with different properties and consequent environmental impacts. Adult zebrafish have shown that TiO2 NPs seem to be less toxic than other metal oxide NPs, toxic effects have been reported after exposure to high doses and prolonged periods stabilized TiO2 NPs that caused mortality 100 mg Ti/L.

Toxicity of silver, gold and platinum nanoparticles in zebrafish embryos;

Nanomaterials are widely used in biomedical applications as carriers for gene delivery, biodetection of pathogens and hyperthermia treatment for tumor destruction. In this study Gold (Au-NP, 15–35 nm), silver (Ag-NP, 5–35 nm) and platinum nanoparticles (Pt-NP, 3–10 nm) were synthesized using polyvinyl alcohol (PVA) as a capping agent. Gold nanoparticles are idyllic for cancer therapy owing to their property to generate heat in the presence of infrared radiation . It is believed that platinum nanoparticles can release platinum ions via surface oxidation, which can contribute to their anti-cancerous properties. Silver nanoparticles are well known for their antimicrobial properties. Ag-NP also induced other significant phenotypic changes including pericardial

effusion, abnormal cardiac morphology, circulatory defects and absence or malformation of the eyes. At 72 hpf, 50% of embryos showed defective eye development at 100 mg/ml of Ag-NP. Both Ag-NP and Pt-NP induced hatching delays**,** as well as a concentration dependant drop in heart rate, touch response and axis curvatures. Au-NP-treated embryos showed normal development with normal heart rate, pigmentation and no abnormal organogenesis.

Toxicity of Iron oxide nanoparticles in zebra fish embryo.

Iron oxide NPs include terabit magnetic storage devices, pigments, catalysis, sensors, high sensitivity biomolecular magnetic resonance imaging, tumor therapy, drug and gene transfer to cells, and labeling of macromolecules and cells. In addition, iron oxide NPs can be used as an adsorbent in the removal of metals from aqueous solutions. The results showed that 10 mg/L of iron oxide nanoparticles investigated developmental toxicity in these embryos, causing mortality**,** hatching delay, and malformation. However, at a concentration of .50 mg/L, the embryos and larvae exhibited severe malformations, characterized by tissue ulceration, pericardial edema, and body actuation.

Toxicity of biodegradable chitosan nanoparticles.

Yu-Lan Hu 2011 et al reported that Chitosan [poly (1,4-β-d-glucopyranosamine)], a natural polysaccharide prepared from N-deacetylation of chitin, has great potential as a biomaterial for the construction of nano sized drug carriers and gene transfer vectors. Several reports have shown that nanoparticles can enter the brain and cause tissue injury. Hence, estimation of the toxicity of these nanocarriers is important for human health.

ZnO nanoparticles used as a positive control to assess the toxicity of chitosan nanoparticles, it was demonstrated that embryos exposed to chitosan nanoparticles exhibited an increased rate of cell death and enhanced expression of reactive oxygen species, as well as over expression of heat shock protein 70 (HSP70), indicating that chitosan nano- particles cause damage to zebrafish embryos. Toxicity was dose-dependent and should be considered at high concentrations. Increased production of intracellular reactive oxygen species was also detected; indicating chitosan nanoparticles caused oxidative stress, as a result of the observed toxicity in zebra fish embryos. In this study, zebra fish embryos were exposed to chitosan nanoparticles for 96 hours, and dose-dependent inhibition of embryo hatching was induced by chitosan nanoparticles of different particle sizes,. Higher expression of HSP70

protein in the nanoparticle- exposed group, indicating stress was caused by the chitosan nanoparticles.HSP70, one of the major heat shock proteins, is usually expressed at low levels, but increases in response to environmental and physiological stressors.

Toxicity of silver nano particles in zebra fish embryos:

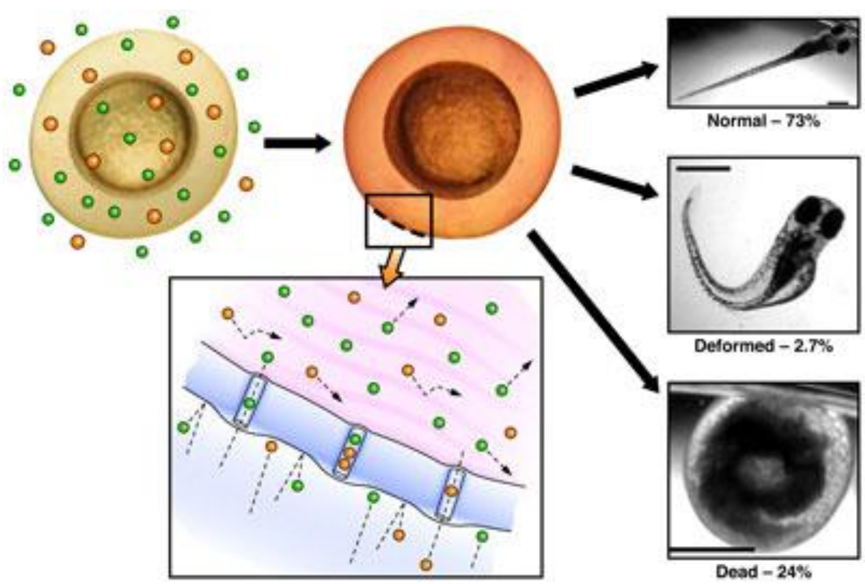
Mansee thakur et al 2014 reported that Nanoparticles are particularly gifted because of their ease of synthesis in various sizes and shapes and they have potential for subsequent conjugation with peptides and proteins for drug targeting. Because of its safe application these nanoparticles are used in therapy and drug delivery. Study about their bioaccumulation and their local or systematic toxicity is essential. This study demonstrates that AgNPs cause developmental embryonic toxicity beyond 1.0µg/ml, resulting in persistent effect on larval behavior; exposure to Ag NPs beyond 1.0µg/ml could be potential hazards factors for biological exposure. Aqueous solution of silver nitrate ($AgNO_3$) taken as source of ionic silver in addition to synthesized silver nanoparticles.In this study Zebra fish embryos were treated with AgNPs (0.0,.3,0.,1.0 and .2.0µg/ml) during 4 to 72 hour post fertilization(hpf). Concentration dependent increase in mortality and hatching delay was observed in Ag NP treated embryos for 1.0µg /ml in almost 90% cases. In this study concentration of or below 0.µg/ml can help prove sustainable to exploit positive effects of nanoparticle application. AgNPs

because developmental embryonic toxicity beyond a concentration of 1.0µg/ml resulting in persistent effects on larval behavior.

Effect of ZnO, CuO, Au, and TiO2 nanoparticle:

Jining liu1 et al 2014 reported that The effects of four different kinds of nanoparticles (NPs), namely, CuO, ZnO, TiO2, and Au, of the sizes ranging from <20 nm to 50 nm on Daphnia magna, early life stage of zebrafish, and various enzymes have been investigated. The experimental results showed that the NPs inhibited both the body length and hatching rate of zebrafish larvae; the small nanoparticles exhibited more toxicity. In the present study, the effects of four NPs, namely, ZnO, CuO, TiO2, and Au, with different physicochemical properties, on crustaceans D. magna and early life stages of zebrafish D. rerio were studied. The activities of three antioxidant enzymes, namely, CAT, SOD, and GSH, associated with the defense system for oxidative stress were also evaluated for biomarker investigation. All embryos hatched successfully in the control group. The hatching rates of the embryos exposed to ZnO NPs (30 nm, 50 nm) and CuO NPs decreased with the increasing concentrations of 1 mg/dm3 to 25 mg/dm3. In addition, no embryo hatched after exposure to ZnO NPs (30 nm, 50 nm) over the concentration range of 50 mg/dm3 to 100 mg/dm3. At 1000 mg/dm3, both TiO2 NPs at 20 nm and 30 nm reduced the hatching success to 5%

and 20%, respectively. At 2.5 mg/dm3, Au NPs reduced the hatching success to 20%.In particular, 30 nm ZnO and 20 nm TiO2 NPs induced more toxicity than 50 nm ZnO and 30 nm TiO2 NPs because smaller particles were more likely to enter the cell.



Schematic of the research findings. Gold nanoparticles accumulate in the embryos. Optical images of zebrafish at a given concentration of gold nanoparticles. (Image: Lauren M. Browning, X. Nancy Xu, Old Dominion University)

Toxic Effects of Silica Nanoparticles on Zebrafish Embryos and Larvae Junchao Duanet al reported that Silica nanoparticles (SiNPs) have been widely used in biomedical and biotechnological applications. Environmental exposure to nanomaterials is inevitable as they become part of our daily life. Therefore, it is necessary to investigate the possible

toxic effects of SiNPs exposure. In this study, zebrafish embryos were treated with SiNPs (25, 50, 100, 200 mg/mL) during 4–96 hours post fertilization (hpf). Mortality, hatching rate, malformation and whole-embryo cellular death were detected. Cellular death assays were performed to determine whether exposure to SiNPs would lead to an increase in cellular death in specific cells or tissues, prior to the overt signs of toxicity shown in Figure 4. Embryos treated with SiNPs exhibited a dose-dependent increase in overall cellular death, significant at higher concentrations (100 and 200 mg/mL). our data showed that exposure to silica nanoparticles caused the inhibition of hatching rate, which led to a direct delay of embryos development. Similar to our findings, delayed hatching observed with carbon nanotubes or nano-ZnO were regarded as an indirect effect of blocking O2exchange [Cheng et al 2007, . Bai W, Zhang Z, et al 2010]. It is still unknown whether the nanoparticles possess specific or non-specific interactions with the chorion. Therefore, more studies are needed to clarify the interactions between the chorion and the nanoparticles.

Conclusion

The increasing use of heavy metals nonmaterial's in catalysis, sensors, environmental remediation and such as commercial products for personal care, there is a strong possibility that these nonmaterial's will finally enter aquatic ecosystems through waste water discharge and washing off recreational activities, such as swimming and water skiing

in this study demonstrate that heavy metals aggregates caused a serious delay in embryo hatching, malformation in zebra fish embryos and larvae and ultimately sudden death condition. Based on the review it can be said that in future with more research and with wider range of heavy metals zebra fish assay can be integrated into teratological and drug toxicity screening programs on a commercial level for the drugs and chemicals before human use. The review collection has been a necessary first step toward developing zebra fish as a model to predict toxicity of heavy metals in humans.

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